Forward engineering neuronal diversity using direct reprogramming.

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Public Summary:

Scientific Abstract:
The nervous system is comprised of a vast diversity of distinct neural cell types. Differences between neuronal subtypes drive the assembly of neuronal circuits and underlie the subtype specificity of many neurological diseases. Yet, because neurons are irreversibly post-mitotic and not readily available from patients, it has not been feasible to study specific subtypes of human neurons in larger numbers. A powerful means to study neuronal diversity and neurological disease is to establish methods to produce desired neuronal subtypes in vitro. Traditionally this has been accomplished by treating pluripotent or neural stem cells with growth factors and morphogens that recapitulate exogenous developmental signals. These approaches often require extended periods of culture, which can limit their utility. However, more recently, it has become possible to produce neurons directly from fibroblasts using transcription factors and/or microRNAs. This technique referred to as direct reprogramming or transdifferentiation has proven to be a rapid, robust, and reproducible method to generate mature neurons of many different subtypes from multiple cell sources. Here, we highlight recent advances in generating neurons of specific subtypes using direct reprogramming and outline various scenarios in which induced neurons may be applied to studies of neuronal function and neurological disease.

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